COMPARATIVE STUDY OF THE EFFECT OF RIFAMPICIN AND TETRACYCLINE IN TOPICAL THERAPY OF TRACHOMA

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C E R T I F I C A T E

This is to certify that the work related to thesis entitled " COMPARATIVE STUDY OF THE EFFECT OF RIFAMPICIN AND TETRACHCLINE IN TOPICAL THERAPY OF TRACHOMA" has been undertaken by Dr. Surendra Kumar Jain under our direct supervision and guidance. The observations and results have been periodically checked up.

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Dated: (SURENDRA JAIN)

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INTRODUCTION

INTRODUCTION

TRACHOMA (rough) an immense subjet, in literature replete with hypotheis, discussion and polemics, in the world pregnant with suffering, disability and blindness, is a specific communicable kerato cunjunctivitis, usually of chronic origen caused by the chlamidia trachomatis. rimarily affecting the superficial epithelium, characterized by the formation of follicles, papillary hyperplasia and pannus, the natural resolution of which is by cicatrization, involving potentially considerable visunl disability. ffecting as it does some 500 million of the world's population, its importance as a source of human suffering, as a cause of blindness and of economic loss all over the world surface in large tracts, is second to none among the diseases of eye.

Among the affected persons most of them are in rural communities of the developing world specially the arid areas of tropical and subtropicalzones there are at least 2 million blind from trachoma and much large number has suffered partial loss of vision. In many communities with endemic trachoma, avoidable blindness and partial visual loss caused by infections malnutrition and cataract impose severe ristraint on economic and social development.

In India trachoma is one of the principal causes of impairment of vision leading to total blindness. It is

estimated that out of 500 millions trachoma cases in the world 125 million are in India alone, there are about 45 million persons in India economically blind out of the world estimate of about 15 million. Trachoma and associated infections are estimated to be responsible for 60% preventable blindness in India.

In recent years the blindness that is preventable and easily unable has been recognized as a public health problem that should be combated the need for prevention of blindness has led to renewal of interest in trachoma and associated infections, which are still most important cause of preventable blindness in the world.

Trachoma is most readily preventable cause of blindness and it commonly co exists with other major causes of avoidable blindness in neglected rural communities. Trachoma controle programme must be gained primarily at those severely affected communities where the disease leads to blindness: In the planning and implimentation of controle programmes. Consideration must be given to simultatneously of other specific measures for dealing the all causes of avoidable blindness.

Since ancient times the drastic measures have been tried for the treatment of the devastating ophthalmia in scourage of conjunctival tissue by copper sulfate even introduction of gonorrheal pus in the conjunctival sac.

Since the advent of antibiotics the treatment has been more effective and less painful. Various chemotherapeutic agents used mainly sulfonamides systemically and tetracycline topically. This topical use of drugs is more acceptable by people, but the method remains less effective as the drugs are not retained in the conjunctival sac long enough.

Recent lab studies have shown that refampicin specially inhibits the trachoma agent after brief exposure to the drug this property should give it a distinct advantage over the other chemotherapeutic agents.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY

The history of trachoma goes back to the earliest medical records and embraces some five millennia. It was known in China where in the time of the Emperor Huang Ti Nei Ching trichiasis was treated in the 27th century B.C.; it was endemic among the Sumerians of Mesopotamia (before 2000 B.C.); and it was a scourge in Ancient Egypt where the evidence of papyri and of forceps used for trichiasis places experience of its ravages at any rate back to the 19th century B.C. (Ebers, 1889). It was also common in Ancient Greece, and in the 5th century B.C. Hippocrates was well acquainted with it, while Heliodorus of Alexandaria wrote a book on the subject in the 2nd century B.C. The classical Romans also knew of it (Pliny and others), and Paul of Tarsus, Cicero, Horace andPliny the younger are believed to have suffered from it. The name trachoma was used by a Cilician physician, Pedanius Dioscorides , Celsus gave a good clinical description of the roughness of the lids and their treatment by rubbing and scarification, while Galen (131-201) and after him aetius of Amida (502-575) fully described the four stages of the disease. In mediaeval manuals Greek and Arab surgeons gave lucid descriptions of its natural history and became adept at dealing with it. There is evidence that it was transported from its natural home in the Middle East

(particularly Egypt -le pais des aveugles, Granger, 1745) from time to time by travellers to be disseminated in other la lands : To Europe by the Crusaders from Palestine; westwards throughout Northern Africa and up into the Spanish peninsula and Southern Europe, and eastwards into Asia as far as the coasts of China by the Moslem invaders; and across to the New World by the Spanish Conquistadores. But the disease was not particularly brought to the notice of European Surgeon and medical research until practically the entire French Army of 32,000 and to a less extent the British , fell victims to it during the Napoleonic campaign in Egypt in 1798-99, and immense numbers of soldiers were sent home blind. From that time dates its introduction to England. Thereafter treatises on the Egyptian ophthalmia appeared by the French military surg eons (Larrey, 1803), while in the English army Vetch (1807) told of how in a battalion of 700 men, 636 were attacked with the loss of both eyes in 50 and of one eye in 90, so that the Government was compelled to make a special outlay in pensions of £ 100,000 for its blinded soldiers, the first pensions ever to be granted. The medical reports are somewhat unscientific, and it is difficult to be precise about accurate pathology; it is certain that some of the cases were of a relatively harmless Koch-Weeks infection, others of a more disastorous gonococcal one, but the description of granulations by some writers (Vetch, 1807)

and the chronicity and cicatricial sequelae in many cases prove that trachomatous infection was widespread (Meyerhof, 1932). The disease, well earning its name of military ophthalmia, was then rapidly spread throughout Europe as a pandemic with appalling results by the armies over-running the Continent at that time and by soldiers discharged in large numbers because of their ocular incapacity, the civilian population becoming secondarily infected as military barracks were emptied of diseased and blinded troops; a military disaster was thus converted into a social calamity of the first magnitude. Thereafter it has remained an international problem.

Although its contagiousness was too obvious to be overlooked, many opinions existed as to the nature of the disease in the early part of the 19th century. Vetch (1807) first stressed the distinctive " granulations" and considered it a specific tissue change resembling intestinal villi; and Mackenzie (1830), describing an epidemic in a French slave-ship which ravaged the Negro cargo, and then the crew and captain so that the ship could with difficulty to brought to port, called the disease granular conjunctivitis, a term adopted by Saemisch (1876) in the first edition of the Graefe-Saemisch Handbuch. Various views were put forward to explain its pathology that it was a proliferation of papillary bodies, groups of small sarcomata, a collection of warts, a herpetic eruption, and so on; but finally Bendz (1858) pointed

out that the essential lesion was composed of accumulations of lymphoid cells so similar to the solitary follicles of the intestine, that he called them lymph-follicles.

A long discussion then arose whether or not such follicles were pathognomonic of trachoma and whether follicular conjunctivitis represented an early stage or an attenuated form of trachoma or was a separate pathological entity. In this heated argument, the unitarian theory was maintained by Raehlmann (1883), Mandelstamm (1883), Rhein (1888), and adovacated by Elschnig (1925), and the dualistic veiw was championed by Saemisch (1879), Sattler (1881), Schmidt-Rimpler (1890), and all modern pathologists. Research along new lines, again involving polemical controversies, was initiated by the finding of organisms by Hirschberg and Krause (1881), Sattler (1881), Koch (1883) and others and thereafter a bacterial, viral or rickettsial cause received adherents. The final chapter concernss itself with the inclusions discovered by Halberstaedter and von Prowazek (1907), a chapter culminating in the successful growth of the causal virus by T'ang and his colleagues (1957) in Pekin and the subsequent verification of their conclusions in many countries of the world. In the meantime, in this century as through the last, despite the activities of researchess, international committees, and nationalprophylactic laws, trachoma continued to increase in incidence with undiminished virulence until comparatively recently when improvements in

hygiene and the gradual dissemination of antibiotic drugs among the inhabitants of the under-developed countries wherein it is endemic are gradually lessening its ravages.

Endemiology- No race isimmune from trachoma, but some are more susceptible than others, and in many countries it is so widespread that it forms an urgent and grave problem of public health. It is frequently asserted that some races are more prone than others, that, for example, the Semitic peoples are readily and severely affected and the American Negroes rarely and lightly; but it is common and often severe in native Africans. Neverthless there is often a considerable ethnic difference in its incidence as is seen in its curiously unequal occurrence in neighbouring communities (such as certain Bantu tribes in Africa of similar social havits some of which are heavily, others lightly, affected, Amies et al., 1953).

The collection of statistical information on the incidence of trachoma was in augurated largely by the influence of Morax; through the League of Nations, La Ligue contre le Tramhoma was founded at the Pasteur Institute in Paris in 1923, and L'Organisaton Internationale de la Lutte contre le Trachome was established by the XIII International Congress of Ophthalmology held at Amsterdam in 1928, while in more recent years many surveys have been conducted by the World Health Organization. The gathering of precise information is a difficult problem and manymethods, none of them

quite satisfactory, have been adopted- the examination of the eyes of school children, of army conscripts, and of samples of the population, the evidence of the statistics of ophthalmic centres, official compulsory notification, and the personal experience and impressions of individual oculists. Much of this information was collected by Wibaut (1929), Sorsby (1950) and Bietti and his colleagues (1962), but, owing to intensive anti-trachoma compaigns, the efficacy of antibiotic treatment in controlling the active stages of the disease, and improved hygiene and medical services in many countries, some of these estimates are now becoming out of date and the infection is becoming progressively less serious as a social meance.

(1) In some countries trachoma has long been practically universal, affecting some 90 to 95% of the indigenous inhabitants in certain areas, notably along the eastern and southern littoral of the Mediterranean, the southern parts of Turkey, the Middle East, areas of Egypt, Libya, Tunsia, Algeria, Morocco and the Gambia.

(2) It is very common, involving from 30 to 60% of the indeginous population of Arbia, Syria, Iran, the Sudan, parts of Greece, large tracts of central and Southern Russia, northern India, China (here more than 100,000,000 were estimated as affected by T'ang , 1934; more than one-third of the total blindness, Shen, 1945), South East Asia manyPacific Islands and large tracts of Central and Western Africa.

(3) It is common, involving at any rate 5% of the population in parts of Italy, Spain (a higher incidence in places), Portugal, Finaland (largely now eliminated), Poland, Czechoslovakia, India (a very high incidence inplaces), Japan, the East Indies, Central America, Mexico, Brazil (a very high incidence in places), and the Argentine.

(4) It is rare generally, but used to occur endemically in certain regions in France, Germany (especially in the east), Austria, Hungry, Ireland, the Netherlands, the United States (especially in a zone through themiddle of the country from the Alleghenies to Kansas and Oklahoma, McMuller and Rice, 1934, and among the Indians), and Australiia (affecting the Aborigines heavily, Mann, 1960). Owing to energetic treatment however, it is rapidly disappearing from many of these areas.

(5) It is rare and sporadic, being mainly but no exclusively confined to imported cases and the foreign population in Britain. Norway, Sweden, Denmark, Iceland, Switzerland, Canada (except for the Indians in the West; Wall, 1934), and New Zealand.

So far as sex is concerned, there is general agreement that a preponderance exists in the female, both in numbers and in seriousness. The commonest age at which the disease is contracted is childhoo. Infants are very frequently infected from their mothers, usually at birth as wellas directly, and in an endemic area the incidence of infantile trachoma is always high; contacts in the street and in school during childhood add the next heavy toll.

In a heavily infected population such as in the Gambia, for example, Collier (1961) found that the incidence in children aged 2 to 4 years is 74% rising to over 90% between the ages of 5 to 9 when the child ceases to be carried on its mother's bak and comes into close physical contact with other children; after the age of 15 when a more adult compertment is adopted, fresh infections are relatively rare.

Although climate does not seem to have a definite influence on the disease, as witness its common occurrence in hot country such as Egypt and a cold country such as Poland or Finland, its incidence seems to some extent to be associated with dryness and dust, and epidemics are usually most rife in the hot months of the year. To a considerable extent in areas such as North Africa and the Middle East this seasonal increase is coincident with epidemics of purulent conjunctivitis caused by such organisms as the H. Oegyptius, and to some extent it can be correlated with the increase in the population of flies which are attracted by purulent exudates around the eyes and serve as vectors in the spread of disease. That flies aided the spread of trachoma in this way was first suggested by Baron Harant ofPoljitz of Bohemia who travelled to Egypt in 1598; their effect in this respect was studied scientificeally by
who spent some time in the
been amply confirmed in
and Abdine, 1952;Ponghi

Finally, as inmost contagious diseases, social status is statistically of fundamental importance for trachoma is overwhelmingly associated with the dirt, squalor, and the intimate proximity of poverty, particularly in regions where the lack of water makes the common washbasin a social necessity and lack of material reduces towels and handkerchiefs to a communal rag.

Aetiology

When it first came into prominence during the Napoleonic campaigns as European pandemic, Egyptian ophthalmia was not considered to be contagious; it was due to the sandiness of the soil, to noxious night vapours, and so on. For long the French surgeons maintained its non contagious nature, and it is to the credit of the British that they recognized it and acted accordingly (Power, 1803; Vetch, 1807; and others). To them it was caused by a putrid animals virus, but even at the Ist International Congress of Ophthalmology held in 1857 it was concluded that certain localities and the nature of the air favoured the incidence and spread of the disease.

Over the next century, however, the evidence became conclusive that the disease was contagious, at any rate in its early stages. It is true that unilateral cases occur (Puscariu, 1934) and the degree of infectivity may be relatively slight in the adult who maintains a reasonable standard of cleanliness (as in the case of a United States physician who did not contract trachoma from his diseased wife until he had been married for 15 years. MacCallan, 1931)

and that in the later (cicatricial) stages of the disease transmissibility does not occur. But long before the causal agent was established it had been proved that trachoma was a contagious disease. During the First World War,for example, hundreds of conscripts of the Russian and Austro-Hungarian Empires escaped military service by infecting their eyes by placing in them rags infected with the secretion of trachomatous patients (Szafnicki, 1923; Taborisky, 1928; and others). Further,there were several reported instances of medical attendants being directly infected by trachomatous secretion from their patients (Wilson,1929; MacCallan,1931; Cuenod and Nataf,1933). Finally, although negative results are on record (Candian, 1933). the literature contains numerous examples of human experimental inoculations wherein the disease was reproduced by inoculating a normal conjunctiva with the contents of trachomatous follicles.

Unfortunately, however,experiments on laboratory animals were relatively unproductive, for most are immune; and further, in those which show a reaction, there are few definite criteria on which a diagnosis of trachoma can be based. None is susceptible except simians, and investigators are by no means agreed as to the experimentally reproducible lesions which constitute the equivalent of trachoma in man. In these, follicles were produced in the conjuctiva particularly of the upper tarsus, by inoculation of trachomatous material; but doubt was thrown on their findings by the discovery that a

transmissible granular condition tends to develop spontaneously in monkeys. More important, the lesions which have been observed in simians (with the exception of Macaca cyclopis which appears to be unusually susceptible, Wang and Grayston, 1962) are by no means typical of human trachoma, differing especially in their benign course and the absence of corneal involvement and subsequent cicatrization: in short; they are typical of inclusion conjunctivitis. Even although there is evidence that the cytological findings in monkeys in the experimental disease may be regarded as having some diagnostic significance (Thygeson et al.,1960). it would therefore seem that animal experiments must be interpreted with reserve, and it is now generally agreed that transference of the disease can only be accepted as unequivocal evidence when it is shown to occur in man.

The infectivity of trachoma being accepted, the nature of the infective agent constituted a problem which exercised men's minds for over a century (see Lindner,1958). Very many theories have been suggested that this or the other organism which had been isolated from cases of trachoma was responsible for the condition .

Innumerable bacteria were described, none of which withstood criticism, but the announcement which excited the greatest interest was by Noguchi (1928) who, examining cases of trachoma among North American Indians, and testing every organism found in the conjuctiva for pathogenic action,found that a bacterium which he named the B. granulosis produced a

follicular conjunctivitis in monkeys which he considered to be trachoma. Initially his findings were substantiated by his associates at the Rockefeller Institute in New York and elsewhere, but soon contradictory evidence began to appear. Attempts to produce a trachoma-like conjuctivitis with B. granulosis proved abortive, both in human beings and in monkeys even when material sent from Noguchi's laboratory was employed . Lindner (1929). indeed was so convinced that this organism did not cause trachoma that he inoculated his own

Sattler (1881). Addario (1905-6), Greeff et al(1907-8), Mijaschita (1908), Nicolle et al. (1911). Taborisky(1928), Michail and Vancea (1932), Thygeson (1933), and others.

In baboons (Hess and Romer,1906),in the orang-outang (Halberstaedter and von Prowazek, 1907), in the chimpanzee and Macacus incus (Nicolle, Cuenod and Blaizot, 1911). and in Macacus rhesus (Noguchi, 1928; and after him many others; see Weiss and Bowers, 1933; Julianelle and Harrison, 1934-35; Hetler and James, 1934).

Hess and Romer (1906), Wilson (1929), Weiss (1930), Kanyo and Rotth (1932).

Wilson (1928-32), Morax (1929),Lindner (1929),Cucco (1930), Rieger (1932), Thygeson (1933), Bland (1944), and others.

Hirschberg and Krause (1881),Sattler (1881),Koch (1883), von Michel (1886),Schmidt (1887),Staderini(1887),

L.Muller (1897), and others.

Olitsky and Tyler (1930), Tilden and Tyler (1930), Olitsky et al. (1931-32).

Wilson (1929) in Egypt; Morax (1929) in France; Bruckner (1928) in Central Europe; Mayou (1928) and others in England; Weiss (1930) and Thygeson (1933) in the United States; Favalero (1932) and Candian (1933) in Italy; Tang (1934) in China; and many others.
conjunctiva with a strain cultured from cases of follicu-losis: a mild follicular reaction appeared in 3 weeks, which completely disappeared in 10 weeks.

A few mycotic organisms have been found in trach-omatous secretions by various authors, none has produced experimental trachoma and all are incidental saprophytes. Similarly, the reports by Busacca (1933-37) and Cuenod and Nataf (1933-37) that louse-borne rickettsiae were the causal agent have not been confirmed.

These negative or inconclusive results naturally led to the search for a virus as the causative agent. Although the earliest attempts to transmit the disease with filtered cultures were unsuccessful in human subjects, positive results in monkeys were reported by a number of authors. This work made it clear that bacteria-free filtrates conta-ining the elementary bodies associated with the inclusions described by Halberstaedter and von prowazek (1907) in Java were causative. The issue, however, became complicated when

Lindner (1909-10) demonstrated that identical bodies were found in inclusion conjunctivitis both of the newborn and the adult, and his suggestion of the close relationship between the two diseases was by no means generally accepted Again, much confusion arose from the multitude of claims by inexperienced trachomatologists that in other conditions similar bodies were found which in reality were incidental artefacts nuclear or cytoplasmic debris, extruded nucleoli or fragments of chromatin, engulfed bacteria or pigment granules. Moreover the inclusion bodies, while not considered specific to trachoma, were not invariably found in trachomatous lesions, particularly when they were quiescent. Despite these confusing factors, it became generally accepted that these bodies were aetiologically related to the disease. They were found regularly in trachoma at the outset of the naturally occurring infection in which, as Wilson (1937) first showed, they were frequently the first recognizable sign; and invariably in the experimental disease wherein they were seen in the incubation period. Moreover, the frequency with which they could be found varied with the severity of the disease, and they were usually present when a chronic condition became reactivated. Again, they were regularly demonstrated in the experimental disease produced in man by bacteria-free filterates of material taken from trachomatous cases; and finally, on an assessment by an expert using accepted techniques, they were never found in diseases other than trachoma- with the exception of inclusion conjunctivits.

For many years, however, attempts to cultivate the organism resulted in failure or, at the most, in claims which led to no pragmatic result and were not or could not be verified in other laboratories. Altogether 18 such were made up to 1957 which have been summarized in the writings of Julianelle (1938) and Thygeson and Nataf (1958), but none of them led to the fulfilment of Koch's postulates or to any material advance in understanding the nature of disease. To fulfil these criteria the typical inclusions with their carbohydrate matrix must be demonstrable in serial cultures, this agent must be shown to produce the typical picture of trachoma with its corneal and conjunctival implications in man, from such an experimental trachoma the aetiological agent must be reclaimed and again grown in serial culture, and the cultivated virus must be avialable for confirmatory studies in other laboratories. All these conditions have now been fulfilled.

Fifty years after the pioneeer work of Halberstaedter and von Prowazek the final chapter of the story began. In Pekin, T'and and his colleagues (1957) succeeded in cultivating the virus in the yolk sacs of 6 to 8 day embryonate hen's eggs by the employment of three fortunate technical dodges: the use of streptomycin itstead of the usual penicillin to eliminate contaminants, for the virus is completely resistant to the former antibiotic; cultivation at 35°C, the temperature of the normal conjunctival sac; and thd systematic

practice of multiple blind passages. The virus so cultivated was found on inoculation into rhesus monkeys to produce a conjunctivitis, in one instance with inclusion bodies. Samples of this virus were sent to London, and here Collier and Sowa (1958) verified the findings of the Chinese workers, improved on their technique, and with a team working in the Gambia, obtained more material in quantity. Finally, at the Institute of Ophthalmology the virus was shown to produce typical trachoma in human volunteers giving rise to characteristic conjunctival and corneal involvement; and in scrapings from these patients inclusion bodies were found and from them the virus was again isolated and grown (Collier et al., 1958-60). This work has now been confirmed in several laboratories in different countries all over the world. The virus has also been cultivated by repeated intracerebral inoculation and passage in mice (Arakawa and Kitamusa, 1950) and in tissue-culture (Furness et al, 1960; Gordon et al,1960; Armstrong et al., 1963) and, as we have seen has been isolated from the urogenital tracts of either sex. The age-long enigma of the aetiology of trachoma is now largely solved.

There is evidence, however, that different strains of this virus exist as shown by their response to antibiotics and their adaptation to mice and tissue-culture (Bernkopf, 1959; Hurst and Reeve, 1960; Furness et al.,1960; Bell and Theobald, 1962). The significance of this is not yet under-

stood. Nor is the relationship of the virus with that of inclusion conjunctivitis generally agreed.

Attempts have been made from time to time to correlate trachoma with some metabolic or constitutional disturbance. Suggestions have been made that it is associated with malnutrition or vitamin deficiency (Winski, 1921; Royer, 1926; Sutton, 1931; Gibson, 1931; and others), but many observations, both experimental (Tilden and Miller, 1930; Kendall and Gifford, 1930; Rice et al., 1934; Hetler and James, 1934) and on the incidence of trachoma in communities in which a deficient diet is common or a diet rich in vitamins is invariable (MacCallan, 1932; Wilson, 1945), Seems to indicate that any such deficiency has no more influence in this than in any other infection. The association undoubtedly arose from the common relationship of trachoma with dirt and poverty and its all-too frequent accompaniment of inadequate food.

Pathology:- The very comprehensive studies which have been made on the histology of trachoma show that it is a chronic inflammation in all the tissue, mucous and sub-mucous, in which the most striking features are the papillary hyder-trophy of the epithelium, a lymphoid infiltration of the sub-epithelial tissues typically with the formation of follicles, and the subsequent proliferation of connective tissue resulting in scar-formation. The whole process is a chronic infective inflammatory change due to a secondary involvement

of the subepithelial tissue following a primary epithelial lesion of both the conjunctiva and the cornea. The papillary hypertrophy is the result of irritation and is present in all long-continued inflammations of the conjunctiva, nor, apart from necrotic changes, is there anything specific in the nature of the follicles; the essential differences between trachoma and other forms of conjunctivitis are the enormous and deeply penetrating subepithelial exudate involving deep tissues such as the tarsus, and the natural termination by cicatrization which results in deformities.

There has been considerable argument whether or not trachoma is an EPITHELIOSIS with strict localization of thee virus to the epithelial cells (Axenfeld, 1914). It has been suggested that since the principal lesions are subepithelial the virus in some form must penetrate to these tissues (Cuenod and Nataf, 1935; Chams et al., 1953), but the fact remains that on histological examination the virus has never been found in any locality other than the superficial epithelial cells, a limitation verified by the electron microscope (Mitsui and Suzuki, 1956). Moreover, virus-containing material capable of exciting a conjunctival inflammation is ineffective both in man and monkeys when injected into the subepithelial tissues through the skin of the lids (Michail and Vancea, 1932; Okamura and Mitsui, 1939; Thygeson, 1951). Similar experiences have been confirmed in inclusion conjunctivitis (Thygeson, 1951). This being so, it would seem

necessary to postulate that the gross subepithelial lesions in trachoma are caused by the liberation of soluble and diffusible toxin such as is known to characterize other members of the PLT group (Mitsui et al., 1954). That such a toxin is indeed present is suggested by the production off a subacute follicular conjunctivitis with pannus and lymph-adenopathy by the conjunctival inoculation of a virus -free ultra-filtrate of trachomatous cultures in human volunteers (Mitsui et al., 1962); that it is lethal to mice on intra-venous inoculation was shown by Bell and his colleagues (1959).

We shall first consider the pathological changes occurring in the upper tarsal conjunctiva since here the disease is seen in its most typical form.

The Epithelium. In trachoma the toxic agent acts upon the entire epithelial layer, conjunctival and corneal. In the very earliest stages characteristic changes are found particularly in the palpebral conjunctiva near the fornix (Taborisky, 1932-33; Wilson, 1937)- cellular division becomes active especially in the deeper layers of the epithelium so that the thickness of this layer increases, while the more superficial cells become flattended and pavement- like, degenerative changes take place in the nuclei and the cells tend to be cast off. Moreover, in the incuba-tion period and during the very early stages the character-stic cell-inclusions are found in the superficial cells.

According to Taborisky (1932-33) these epithelial changes transformation of type, nuclear degeneration, proliferation and exfoliation- are characteristic of trachoma; apart from the presence of inclusion bodies, which can always be found at this stage if looked for with sufficient care, he has claimed that a histological diagnosis can thus be made in the first few days of the disease.

These epithelial changes progress as the disease develops. The proliferative tendency becomes marked and PAPILLAE are formed, the cells tending to maintain their characteristics in the depressions, but becoming many-layered and flattended on the summits where the superficial cells readily become exfoliated. In this activity the basal cells become cubical or cylindrical and show many mitotic figures, and the overgrowth may lead to the formation of cockscomb-like sprouts. Short solid, or long tubular epithelial downgrowths may penetrate deeply into the structure of the lid, so that finally buried epithelial islands may be left in the cicatrical tissue (Lamb, 1935). Frequently the solid downgrowths degenerate centrally and the ducts of the tubular " glands " become compressed and strangulated by the dense cellular infiltrate largely made up of plasma cells, so that in either case pseudo-cysts are formed; these give an adenomatous appearance to the deeper layers while the cysts are often filled with epithelial debris which may undergo calcareous degeneration to give rise to concretions. These changes are not pathognomonic of trachoma and tend to occur in many chronic irritations of the conju-

native, but they are not found in simple follicular conjunctivitis.

Other subsidiary changes abound. Goblet cells increase, and these, accumulating in the downward-growing sprouts of epithelium, may lead to the formation of retention cysts. As the folds and furrows increase- so much that Berlin (1878) and Iwanoff (1878) mistook them for specific "trachoma glands" these distension cysts may become numerous and large; the central cells degenerate, the peripheral ones gradually become flattened, the lumen becomes distended with mucus, loose epithelial cells, inflammatory cells, and other debris, and an inflammatory thickening of the surrounding fibrous tissue may form a peseudo-capsule the whole, together with the crypts and crevices, forming an excellent nidus for continuing the infection and constituting an obstacle in eradicating the disease.

In the acute stages the epithelium is crowded with lymphocytes, leucocytes and plasma cells; but in the more chronic stages it becomes attenuated and thin, showing no characteristic changes. Finally, it tends to develop epidermal characteristics, with prickle-cells and a horny superficial layer. Hyaline, amyloid and xerotic changes have also been described.

The Submucosa. In the very early stages of the disease all elements of the subepithelial tissues take part in the general hyperplasic process; a capillary dilatation occurs associated with a diffuse infiltration with lymphocytes and plasma cells, while mononuclears and

histiocytes begin to collect in places. Intense proliferation is evident among the endothelial cells of the capillaries and lymphatics, with the formation of lymphoblasts and mature lymphocytes in quantity; and gradually in the general infiltration, follicles begin to be formed. It is to be noted that although follicular formation is characteristic, it is not invariable, for some cases may show a generalized infiltration without any tendency to its aggregation into follicles the general infiltrative type as opposed to the follicular type (Michail, 1921; MacCallan, 1936). At the same time the hyperaemia and inflammatory oedema in the mucosa lead to the formation of vascularized papillae which get secondarily infiltrated with lymphocytes and other cells.

In the submucosa the general cellular infiltration eventually contains, in addition to the preponderating lymphocytes, elements such as eosinophils and mast cells in considerable numbers especially deep in the tissues, plasma cells in enormous numbers especially under the epithelium, wandering through it and into the discharge, an occasional large macrophage, and relatively few polymorphs, usually aggregated in heaps and usually associated with secondary infection. Traversing the cellular elements are many connective -tissue fibres, the fibroblasts having their origin from the adventitial cells of the blood vessels, and eventually a fine reticulum of lattice-like connective-

tissue fibres may be fully developed (Kruckmann,1932; Peters,1932).

The papille may be present in extraordinary numbers and reach a high state of development,particularly above the limit of the tarsal conjunctiva: over the tarsal plate the fixation of the tissues hinders swelling and hypertrophy and the surface is merely roughened with short papillae, but in the fornix , especially in the region of plateaux and furows, large plump papillae and even cauliflower growths are formed . In their stroma are numerous dilated blood vessels, and dilated lymphatics packed with lymphocytes. As the new vessels grow and capillary loops sprout out, new connective-tissue cells appear, and at an early stage fibroblasts have already developed from the adventitial cells (Birch-Hirschfeld,1925); when these contract the papillae shrink, although their position is marked for a long time by deep folds.

The FOLLICLES are the most striking part of the histological picture. Initially they appear as scattered aggregations of lymphocytes, with some mononuclears, plasma cells and histiocytes fading off into the surrounding cellular infiltration. As the follicle forms, its central part is made up of a mass of mononuclear cells and histiocytes with a few scattered lymphocytes; in addition the actively phagocytic cells of Leber are prominent, sometimes reaching enormous proportions,containing ingested

material in various stages of digestion. The cortical area is made up of a zone of lymphocytes showing active proliferation, at first fading off into the neighbouring subepithelial infiltration but later surrounded by an incomplete layer of flat elongated cells simulating an endothelial lining but composed of fibroblasts stretched by the pressure of the enlarging follicle; there is no true capsule although a semblance of such a structure may be created by the compression of the surrounding connective tissue and commencing fibrosis. Blood vessels are always found in the periphery whence sparse thin-walled capillaries may penetrate towards the centre, and from their adventitial cells an indefinite network of reticular fibres may spread, particularly near the periphery; no true connective tissue stroma exists. As the follicle ages the central cells stain poorly, many of them obviously degenerating and undergoing autolysis, while the spaces between them are occupied by homogeneously staining eosinophilic material, probably of the nature of exudate. According to Thygeson(1955) and Kimura and Thygeson(1955) the follicles of trachoma are differentiated from all others by these signs of necrosis, for in expressed material are found cytoplasmic debris, cells with bare nuclei and the large macrophages which act as scavengers to remove brokendown cellular material. Occasionally some follicles become confluent so that large masses are formed made up histologically of many follicles which may grow to form tumours with several lymphoblastic centres

The fate of the follicles varies. Occasionally they may disappear without trace, sharing in a general resolution of the inflammatory process. Sometimes a superficial follicle ruptures spontaneously or on slight trauma, evacuating itself so that the resulting wound heals by cicatrization ; more usually, however, they gradually disappear by resolution and atrophy in the process of subepithelial cicatrization. The connective-tissue reticulum at the periphery proliferates and spreads centrally so that the blood vessels are obliterated and the central cells necrose, their nuclei losing their stain and the cytoplasm becoming granular until eventually the whole breaks down into an amorphous mass to be replaced in the end by compact scar-tissue.

Cicatrization. Searring of some degree is always present, sometimes from a very early stage, but in its pathology there is nothing specific. It is of the usual inflammatory type; its extent is its only characteristic. It arises from the diffuse hypertrophy of the connective-tissue elements which have their origin in the adventitial cells of the blood vessels(Addario,1900; Kruckmann, 1932). The process occurs over the whole submucous fissue and embraces a proliferation of connective-tissue, its contraction and a strangling of the blood vessels with the eventual formation of compact scar-tissue. Occasionally in the mildest cases a few delicate cicatrices may

be all that is visible, but, in the worst cases, fibrous tissue may replace the follicles and the entire infiltrated subepithelial layer, often leaving islands of infiltrated tissue for some time within its interstices. In other cases degenerations, typically hyaline, but also fatty, amyloid or even calcareous, may develop, producing the ''gelatious'' types of trachoma. Meantime the epithelium becomes taut, atrophied, and stretched over the scar-tissue, and may become epidermoid and xerotic, contraction occurs, deformities are produced, and the fornices themselves may be almost completely obliterated. Krause's glands are drawn forwards towards the middle of the lid, become infiltrated and atrophied and finally cyst-like, and the infiltration may extend so deeply into the loose tissue of the fornix as to involve the muscle fibres.

At the stage of scarring when the follicular elements have been obliterated, fibroblasts occupy the main bulk of the tissue, but there is usually a perivascular infiltration of polyblastic histiocytes and plasma cells with a few lymphocytes, eosinophils and basophils (Lumbroso, 1933). Occasionally in the upper lid a massive hyperplasic infiltration occurs producing a tumour-like mass, the most usual element of which is plasma cells resulting in the formation of a plasmoma (Pascheff, 1932; Ernyei, 1933; Cattaneo, 1934; and others). Derkac (1934).

described four cellular types of such tumours - a hyperplasia of plasma cells, of lymph cells, of histioblastic cells of reticuloendothelial origin, and a purely fibrous type.

These changes occur typically in the conjunctiva of the upper lid, particularly in the fornix: to a less extent they involve the lower lid, the plica, and the caruncle, and in a more specialized way the tarsus, the bulbar conjunctiva and the cornea.

The tarsus in the early stages of the disease is succulent and thickened owing to a cellular infiltration of round cells and mast cells, which may penetrate deeply into it: the infiltration may be general but sometimes is patchy and relatively small (Wilson, 1937). The subsequent degeneration and softening leads to deformation - a primary affection of the tarsus, rather than a mechanical deformation secondary to contractions ofthe mucous membrane. The tarsal glands are affected to a variable extent. Sometimes they show little or no change; at other times, partly owing to atrophy, partly to strangulation first by the dense infiltration and later by scar tissue, the acini degenerate into cystic spaces, the lining epithelium degenerates, sometimes to be replaced by many layers of cells, hyaline and fatty changes set in, and finally in place of glands only groups of fat cells may remain. It is important that the disease may linger here for some considerable time raising the possibility of re-infection (Zykulenko, 1933;

Pulvertaft, 1935). Frequently the edge of the lid is invaded and the glands of Moll are implicated, resulting in hyperplasia and cyst formation.

The bulbar conjunctiva had for long been considered to be relatively free from the trachomatous process (Raehlmann, 1883-1903), but its clinical appearance is deceptive. Underneath the apparently normal conjunctiva there is a cellular infiltration, especially of plasma cells, usually with cellular accumulations in the region of the blood vessels, and sometimes with the formation of true follicles which, however, tend to absorb without cicatrization (Bietti, 1903; W. and M. Goldzieher, 1906; Ichikawa, 1911; Kreiker, 1921; Pascheff, 1932). The disease is less fully developed than in the palpebral conjunctiva, but it may attack the bulbar conjunctiva first, and the evidence points to the fact that it is a primary infection and not a mechanical contact infection from the upper lid.

The cornea exhibits some of the earliest and most typical changes of trachoma in the appearance of a superficial keratitis and the eventual formation of PANNUS TRACHOMATOSUS. The earliest changes are detectable by the slit lamp contemporaneously with the appearance of the first signs of inflammation in the tarsal conjunctiva (Wilson, 1932) while some degree of pannus is present in every case of trachoma. These facts indicate that the infection of this tissue is specific and primary, not secondary and incidental.

The initial changes in the acute stage occur in the epithelium, taking the form of a diffuse epithelial opacification with punctate epithelial erosions leading to the development of an avascular punctate epithelial and subepithelial Keratitis (Busacca,1933): an oedema of the epithelium occurs and an infiltration with polymorphonuclear leucocytes together with the appearance of the intracellular inclusions (Taborisky,1914,Kaufman, 1960). Even at this stage Bowman's membrane may be attacked and broken up into layers between which polymorphs accumulate. The picture suggests a primary attack on the corneal epithelium by the virus, and the subsequent vascularization and pannus-formation may with some reason be considered a defence reaction by a normally avascular tissue against the attack of the virus.

Following the epithelial disturbances, changes occur in the terminal capillary zone of the limbal system of vessels which develop into a trachomatous pannus. The capillary loops become dilated, elongated and more irregular, and are surrounded by an oedematous cuff (Galante,1934). Secondarily to the vascular neoformation, a cellular infiltration of lymphocytes and a smaller number of plasma cells produce a cloudy opacity, and as this descends, parallel non-anastomosing vessels follow in its wake. These new-formed vessels begin as endothelial rods and remain with fine endothelial walls with

sometimes a coating of connective tissue, insinuating themselves between Bowman's membrane and the epithelium, an indication that the neovascularization is due to direct infection of the latter. In the later stages they appear under Bowman's membrane as well, so that a large part of the thickness of the substantia propria is involved, and eventually the membrane is perforated freely and ultimately may be destroyed. In the pannus, typical follicles are found, especially near the limbus . They are found in all stages of the disease, but usually in the stage of regression. Histologically they are identical with those seen in the conjunctiva and are surrounded by a vascular network. Meantime, in the epithelium secondary changes are taking place. The surface becomes uneven, thickened and irregular, wandering cells invade it, exfoliation occurs, and aided by the mechanical rubbing of the rough upper lid, intractable ulcers are prone to develop. At the limbus a considerable hypertrophy occurs, and, as in the tarsal conjunctiva, downward-growing sprouts dip into the subepithelial tissue, giving the appearance of glands.

When the pannus regresses sclerosis sets in, and as the follicles cicatrize, the epithelium reconstitutes itself and fills up the spaces where the resolved nodules formerly existed (Busacca,1935). In the less severe cases the pannus may disappear, leaving the cornea practically

clear but with fine vessels in it; in the more severe cases permanent cicatricial tissue remains.

SYMPTOMS

The onset of trachoma is often inapparent or gradual and, in children, may not be noticed by the parents. In mild cases the patient experiences slight ocular discomfort some watering of the eye, minimal sensitivity to light, the sensation of having a foreign body in the eye, and a little purulent discharge in the morning. In severe cases with marked involvement of the cornea, the photophobia and watering are much more marked and may cause children to avoid the light whenever possible. Unless there is an associated bacterial infection, trachoma does not cause a copious purulent discharge. In severe grades of chronic trachomatous inflammation, the symptoms are often far milder than would be expected from the clinical findings.

Patients with trichiasis and entropion experience constant pain and discomfort from the inturned eyelashes that abrade the cornea, and they often seek temporary relief by plucking out the lashes. Corneal ulceration that develops as a complication of the inturned eyelashes produces severe pain and marked photophobia.

Clinical signs

Conjunctiva and lids - In the early stages, trachoma appears as a follicular conjunctivitis, with papillary hypertrophy and inflammatory infiltration involving the whole conjunctiva and most characteristically the upper tarsal conjunctiva.

Conjunctival follicles are elevated granules with a vascular centres that may be yellowish to grey-white or translucent. They very from 0.2to 2 mm in diameter. Histologically, they consist of lymphoid tissue with germinal centres.

Papillary hypertrophy, which is characterized by vascular engergement and inflammatory infiltration, occurs where the conjunctiva is tightly bound down to the underlying tarsal plate. At first there is an engergement of the smaller vessels, which appear as red dots on the tarsal surface of the conjunctiva. This is accompanied by conjunctival thickening due to infiltretion, which obscures the deeper vessels that r-un vertically in the upper tarsus,(severe cases these vessels may be completely hidden. In cases of atopic (or allergic) conjunctivitis, the papillary hypertophy typically progresses to the formation of " giant " or " cobblestone papillae " that are polyp-like, confluent masses of conjunctiva.

As trachoma progresses, cicatrization of the conjunctiva appears as fine linear and small stellate scars in mild cases and as broader confluent or synechial scars in more severe cases . Although scarring commonly progresses during the resolution of conjunctival inflammation, some cases with marked conjunctival scarring may continue to have severe, active disease with follicles and infiltration for many years.

The major, potentially blinding sequelae of trachoma are distortion of the lids (particularly the upper lid), trichiasis (misdirection of the lashes), and entropion (inward

deformation of the lid margin).The abrasion of the cornea by eyelashes, especially when aggravated by even a minor foreign-body injury or by deficiency in tear secretion, frequently results in corneal ulceration, followed by scarring and visual loss, Inadequate wetting of the cornea (tear-deficiency syndrome) and stenosis of the lacrimal outflow ducts are other late complications in patients with severe scarring. Following severe and deep trachomatous conjunctival inflammatory disease in the upper fornix, fibrosis of Muller's muscle may lead to defects in lid closure, which may be aggravated by notching of the lid margin or by deficient tear secretion. These gross disorders of the normal protective mechanisms predispose to traumatic and secondary infective damage to the cornea.

Cornea - Corneal lesions in trachoma include punctate and diffuse epithelial keratopathy with punctate erosions of the epithelium, small cellular infiltration of the corneal epithelium and anterior stroma, superficial neovascularization (vascular pannus), shallow peripheral ulcers, swelling of the limbus (corneal-scleral border), and the formation of lymphoid follicles at the limbus which resolve, leaving characteristic depressions (Herbert's pits). Typically, the epithelial keratitis of trachoma occurs more commonly in the upper half of the cornea, although it is not limited to this area. Inflammatory infiltrated of the cornea range in size from lesions so small that they can be seen only with a slit lamp to large trachoma pustules. The trachoma pannus consists of a superficial fibrovascular membrane extending over the

surface of the cornea from the limbus. In the active stages, there is diffuse and focal infiltration between and beyond the newly formed vessels; this infiltration resolves, leaving varying degrees of opacity due to scarring. The opacity is usually more marked on the superior cornea, although it is present all around the limbus and may extend across the cornea.

In addition to the specific trachomatous involvement of the cornea, there is a high prevalence of other corneal disorders in trachoma endemic populations. Superficial corneal scars in association with the corneal vascularization are very common even in children and may be the result of trauma, infection or malnutrition. Bacterial ulcers of the cornea, initiated by damage caused by trichiasis, entropion, foreign bodies or other injuries, are frequent in communities with blinding trachoma, especially at times of epidemic acute ophthalmia.

Potentially disabling and disabling lesions

The potentially disabling, irreversible lesions are (1) distortion of the eyelids due to conjunctival scarring (C_3)& (2) trichiasis and/or entropion (T/E). Previously, trichiasis and/or entropion were recorded as conjunctival scarring, grade 4 (C_4). To emphasize disabling lesions and to provide a more direct indication of the risk, it is useful to record trichiasis entropion separately from conjunctival scarring.

The disabling lesion is severe central corneal scarring with gross visual loss (CC_3).

The scores for these irreversible lesions, as given below, represent a slight modification of those originally proposed by Dawson et al. (11).

Conjunctival Scarring (C):

C_0 No scarring on the conjunctiva.

C_1 Mild: fine scattered scars on the upper tarsal conjunctiva, or scars on other parts of the conjunctiva.

C_2 Moderate: more severe scarring but without shortening or distoration of the upper tarsus.

C_3 Severe: Scarring with distortion of the upper tarsus.

Trichiasis and/or entropion (T/E):

T/E_0 No trichiasis or entropion.

T/E_1 Lashes deviated towards the eye but not touching the globe.

T/E_2 Lashes touching the globe but not rubbing on the cornea.

T/E_3 Lashes constantly rubbing on the cornea.

Corneal scarring (CC):

CC_0 Absent

CC_1 Minimal scarring or opacity but not involving the visual axis, and with clear central cornea.

CC_2 Moderate scarring or opacity involving the visual axis, with the pupillary margin visible through the opacity.

CC_3 Severe central scarring or opacity with the pupillary margin not visible through the opacity.

Blinding and non-blinding trachoma

A community with blinding trachoma can be recognized by the presence of persons with severe visual loss due to corneal opacity and a substantial prevalence of potentially disabling trachomatous lesions, particularly trichiasis/ entropion. These irreversible changes appear as the long-term outcome of prolonged or recurrent inflammatory disease of moderate or severe intensity. Communities with non-blinding trachoma may have a low prevalence of potentially blinding lesions, and do not have a substantial prevalence of trachomatous visual loss.

In communities with active, blinding trachoma, chlamydial infection is always present but other ocular microbial pathogenes appear to contribute significantly to the intensity of trachoma and to the lesions that impair vision. From the public health point of view, trachoma is important as a cause of preventable blindness. The failure eto distinguish communities with blinding trachoma from those where it is present but not bliding leads to confusion in determining priorities and in selecting areas for control programmes.

Classification of trachoma by stages (after MacCallan)

Trachoma cases are usually classified in four stages originally described by MacCallan (13). This classification, based only on conjunctival findings, described the evolution of the disease, but does not have prognostic value.

Tr I Trachoma stage I : Trachoma at onset.
Immature follicles present on the upper tarsal conjunctiva. Early corneal changes are susually present.

Tr II Trachoma stage II : Established or florid trachoma.
Presence of well-developed mature soft follicles with papillary hypertrophy and diffuse infiltration. Associated corneal findings may include pannus and infiltrates extending from the upper limbus and limbal follicles of Herbert's pits.

Tr III Trachoma stage III : Cicatrizing trachoma.
Conjunctival scarring is present with some of the conjunctival signs of stages I or II.

Tr IV Trachoma stage IV : Cicatrized or healed trachoma.
Inflammatory signs in the conjunctiva have resolved but scar tissue remains. The disease is no longer infectious, although further changes in the scars may follow.

The term "trachoma dubium" has been used to indicate cases that were thought to be early trachoma but lacking sufficient signs to make the diagno-sis.

" Mature" follicles have been defined as "soft", "necrotic", "liable to rupture under light pressure ", and " leaves a conjunctival scar ". In practice these definitions are difficult to apply so that, in field surveys, observers

frequently differ in the classification of individual cases as Tr I or Tr II. In mild cases, it is often difficult to differentiate Tr I and Tr III from Tr IV, i.e. to distinguish mild active disease from inactive disease. Thism may lead to variation in the classification of cases by stages by different observers, but these mild cases do not represent significant degrees of activity in terms of infectivity for others or risk of loss of vision.

Furthermore, the MacCallan classification does not identify the varying degrees of inflammation or the cases with (or at risk of developing) visually disabling lesions. For this reason it is necessary to evaluate endemic trachoma in terms of communities with blinding or with non-blinding trachoma. This evaluation is based on the presence of severe signs of follicular, papillary and diffuse inflammatory reaction (i.e. the intensity of inflammatory disease), conjunctival scarring, trichiasis/entropion, and corneal scarring, as described above.

DIAGNOSIS OF TRACHOMA

Diagnosis in the field :- When there is uncertainly concerning the presence or absence of trachoma in a given community or area, it is essential to use strict diagnostic criteria that are unlikely to yield false positive interpretations. For this purpose, individual cases must have at least two of the following signs.

1. Follicles on the upper tarsal conjunctiva.
2. Limbal follicles or their sequelae, Herbert's pits.

3. Typical conjunctival scarring.

4. Vascular pannus most marked at the superiorlimbus.

Herbert's pits are the only clinical sign unique to trachoma, but they do not occur in every case. Their presence is sufficient indication of previous trachoma.

On the other hand, once the presence of endemic trachoma has been established, it is desirable to use more sensitive but slightly less specific criteria for diagnosis; in surveys to measure endemicity, the presence of one of the above signs in individual cases is sufficient.

Differential diagnosis - There are a number of conditions that may pose a problem in differential diagnosis of individual cases. The forms of chronic follicular conjunctivitis, other than those caused by chlamydial infection orchronic bacterial infection (which merge in endemic trachoma), are

1. Folliculosis

2. " Toxic " follicular conjunctivitis induced by :

   (a) Molluscum contagiosum

   (b) topically applied drugs

   (c) eye cosmetics

3. Bacterial : caused by Moraxella species and other bacteria.

4. Axenfeld's chronic follicular conjunctivitis.

5. Chronic follicular keratoconjunctivitis of Thygeson

6. Parinaud's oculoglandular syndrome.

These conditions are either rare or present little risk to vision.

Cases of vernal catarrh occur occasionally among children in trachomatous communities. These cases are frequently diagnosed as active trachoma because of their marked papillary hypertrophy. In communities with a high level of active trachoma requiring chemotherapy, the inclusion of these cases among those to be treated is advisable because they also often have trachoma. Chemotherapy should not be withheld because of uncertainty in diagnosing active trachoma in the presence of vernal catarrh. On the other hand, the chronic progression of trachoma under inappropriate steriod treatment given for erroneously diagnosed vernal disease is a common event in some areas, and should be avoided.

Role of laboratory tests

Laboratory tests are not essential in trachoma control programmes. However, they may be used for a number of reasons: to support the clinical diagnosis of the disease in individual cases; to measure the prevalence of the infection in a community where trachoma is endemic (i.e. to estimate the "force" of infection); to monitor individuals or communities for the effect of therapy; to estimate the total exposure of a population to chlamydial infection; to monitor for shifts in serotypes in a given population which might indicate influx of the agent from outside the community or possible transmission from a genital reservoir.

Laboratory procedures to detect the presence of chlamydiae in trachoma cases include :

- microscopic examination of Giemsa- or immunofluorescent stained conjunctival smears;
- isolation by inoculation of specimens into special tissue culture systems or into the yolk sac of embryonated eggs;
- detection of specific antibodies by microimmunofluorescence (micro-IF), complement fixation or other tests.

These procedures are described in the Guide to the Laboratory Diagnosis of Trachoma, published by WHO in 1975 (17). A further simplification of tissue culture methods for use in the field was described subsequently (14).

Bacterial studies should be an integral part of the laboratory evaluation of individuals or communities with trachoma. The more important ocular bacterial pathogens include Haemophilus sp., pneumococcus, Neisseria sp., Moraxella sp. and Staphylococcus aureus; other pathogens such as Gram-negative rods and beta-streptococci are less frequent. The most commonly used method to detect bacterial pathogens in trachomatous populations is the examination of Gram - or Giemsa-stained conjunctival smears. However, appropriate culture techniques such as isolation on blood agar may be more sensitive and specific.

TREATMENT It is only within recent memory, with the advent of chemot herapeutic and antibiotic drugs, that trachoma has become a treatable disease; its prophylaxis by immunological methods is still an unrealized possibility. It is now fully established that the sulphonamides, the tetracylines and

erythromycin are highly active therapeutically, that penicillin and chloramphenicol are active but to a less extent and that streptomycin is inactive, while most strains are insensitive to polymyxin, neomycin, viomycin, gramicidin, ristocetin and bactracin. The sulphonamides are best given systemically, the antibiotic drugs topically, and the two methods can be combined when a maximum effect is desired; where structural damage has not occurred rapid resolution can be expected, although it is to be rem-embered that when considerable hyperplasia has occurred, a minimum period of 3 months must elapse before it can be expected to disappear even in the absence of virus. Any clinical assessment of cure must therefore a wait this period. Refractory cases commonly occur, and these should receive a further course of treatment, preferably with a change of drug and with a combination of systemic and topical treatment. When the disease is advanced and considerable hyperplasia exists, treatment may be facilitated by the expression of gross follicles or bleb-like excrescences, or by the excision of grossly infected tissues; while in the cicatri cal stage the operative correction of deformities, particularly for trichiasis, may be indicated. Cure can be measured by the absence of follicles, of epithelial keratitis, of corneal infiltration so that the vessels of the pannus are left bare, of conjunctival hyperaemia and roughness even in the presence of scars, by negative findings in scrapings or biopsies, and by failure to cultivate the virus. Finally, when pannus has

left the cornea opaque, keratoplasty may do much to restore useful vision (Paufique and Charleux, 1964).

While individual cases should be treated intensively with systemic sulphonamides or effective topical antibiotic drugs at a concentration of 1.0% in ointment or oily suspension twice or thrice daily for 2 to 3 months, different techniques may be advisable in mass campaigns in endemic areas where constant treatment of individuals may be impracticable. In these circumstances the most rewarding technique is the administration of a long lasting sulphonamide, supervised, for example, by teachers in the case of schoolchildren (sulphamethoxypyridazine, sulphaphenazole or sulphadimethoxine given twice a week for 3 months, the dose not to exceed 80 mg. per kg. of body weight per week), or topical tetracyclines given in oily drops in intermittent courses (twice daily for 6 consecutive days each month for 6 months; see Reinhards et al. 1959; and others).

Before the introduction of the sulphonamides in 1938 no specific treatment for trachoma was known was known and the only expedient was to destroy the diseased tissue (and the virus) and thus render the disease inactive. The inefficacy even of the most careful treatment of this type was seen in the case of surgeons whose eyes had been accidentally infected and immediately treated drastically, and, despite this progressed to a severe intractable and prolonged illness (Clausen, 1916; MacCallan, 1931; and others). As we would

except in a widespread disease the origin of which long remained in obscurity and the termination of which was in the grave, innumerable methods of treatment were constantly being proposed. Despite the number of suggested remedies, most experienced ophthalmologists relied essentially on the agent used by the early Egyptians, Greeks and Romans to destroy the active infection which had been the sheet-anchor in the treatment of trachoma throughout the ages- COPPER, most effectively used as "blue stone," a pointed crystal of copper sulphate held in a wooden holder. With this the lids were scoured daily, month after month, year after year, until the disease became quiet. The process was by no means painless, nor was it rendered so by cocaine; but half-measures were useless. It is a fairly true generalization to say that every case treated thus from the beginning eventually became inactive, although the process took several years. Too early cessation of the treatment invariably ended in relapses, and too frequently several such relapses ended in an incurable condition.

While copper formed the basis of treatment for trachoma our ancestors were driven to even more drastic procedures in the grosser types of disease, particularly when a pannus crassus developed. Friendrich von Jager, for example, about 1812, introduced treatment by the inoculation of the eye with gonorrheal pus from the genitalia or cases of ophthalmia; his technique was widely followed by Piringer (1841) in Gratz, Wharton Jones (1847) in England, and Warlomont (1855) in Belgium; in

England the treatment was usedby Bowman, and Bader (1863-64) reported on 170 cases at Moorfields Eye Hospital, While a somewhat reluctant early advocate in the United States about 1860 was Elkanah Williams of Cincinnati. The immediate reaction was drastic and often catastrophic, but although some eyes perforated and were lost, many survived, often with a remarkable clearing of the pannus and the restoration of some vision. The technique was generally abandoned when de Wecker (1882) introduced the more readily controllable chemical irritant, jequirity (abrin) into ophthalmic practice.

Other methods of therapy based on similar principles were found to be less effective- silver nitrate, alum, lotions of mercuric chloride, chaulmoogra oil, Jodine, subconjunctival injections of cyanide of mercury and dionine, and a host of others, as well as radiation with ultra-violet light or X-rays.

When the granulations or bleb-like excrescences are exuberant in established cases, much time may be saved by their mechanical destruction, but this is rarely required with modern methods of therapy. For this purpose Knapp's (1892) method is effective: his roller forceps is closed upon the everted lid, one limb being in the fornix and the other on the tarsal conjunctiva, and these are pressed together and drawn firmly across the fornix, the blebs in this region being expressed ; those near the angles and any left over in the tarsal region can be expressed with ordinary forceps or scooped out with a sharp spoon, sometimes more easily after incising them with a knife. Scarification with a knife and subsequent

massage with antiseptics were recommended by Rasevi (1895); groups of granulations could be attacked with the galvano-cautery (Kern, 1870; Samelsohn, 1873; and others), a pencil of carbon dioxide snow (cryotherapy[Harston, 1911; Sjogren, 1930), or diathermy (Kalloch, 1927; Monbrun, 1929; Ragain, 1929; von Grolman, 1935; and others).

When the whole palpebral area was grossly diseased excision of the fornix, and sometimes also of the tarsal plate, used frequently to be practised. The excision of diseased areas was a procedure known to Hippocrates, but it lapsed until it was revived by Saunders (1811), Adams (1817) Rust (1820), von Walther (1821) and more enthusiastically by Heisrath (1882), and was finally established by Kuhnt (1897). Today, however, it is rarely required except in long-standing cases wherein the tarsus is heavily diseased. Similarly the transplantation of mucous membranes practised by Dening (1911), a procedure essentially designed to quieten a persistently active pannus, has fallen into desuetude. Special treatment for the pannus is as a rule unnecessary as it tends to regress with the conjunctival condition; the most that is required in the few cases wherein specific measures seem advisable is a peritomy augmented by destruction of the vessels by the galvano-cautery or diathermy.

The complications of trachoma should be treated on general surgical lines-ulcers, iritis, and so on. Trichiasis must always be dealt with, and until this can be done satisfa-

eterily relief can be obtained with a contact glass. If the inturned lashes are few, electrical epilation may be attempted but it is rarely indicated as the trichiasis is usually widespread and because the distortion of the roots and the irregular out-sprouting of new lashes always make it difficult and frequently impossible to destroy them satisfactorily. A better alternative is a drastic operation such as the interposition in the free border of the lid behind the lashes of a mucous membrane graft from the lips, as in van Milligan's operation, or the eversion of the lower part of the lid by the removal of a wedge-shaped strip of tarsus, as in Streatfeild's operation; if the tarsus is grossly deformed it may in great part be excised. If blepharospasm exists a cantheplasty is indicated. When xerosis develops amelioration is difficult; emollient drops should be frequently instilled, and very considerable relief and improvement in the corneal transparency can be obtained by a tarsorrhaphy at each canthus leaving a small central slit only. A transplantation of Stensen's duct was advocated by Paufique and Charleux (1964).

From the prophylactic point of view in endemic areas vaccine treatment of the child population would be the method of choice and might eliminate the most serious social aspects of this disease. Collier (1961) showed that baboons could be protected from inclusion conjunctivitis by a live vaccine when challenged by conjunctival inoculation with the same strain, and Bietti and his colleagues (1961-63) that the same applied to man using a vaccine prepared from a trachoma

MATERIAL AND METHOD

MATERIAL AND METHODS

Patients

The patients included in this study were the children from the primary schools of Bundelkhand rural area. Children included were all from the 5th standard ranging in age from 9-12 years of both sexes. 232 patients were examined clinically and 141 were found having active trachoma in different stages. 100 out of them are selected for study and divided in two groups of 50 each including almost equal amount of severity groups.

Clinical Examination

All clinical observations were made in the help of a torch and binocular loup the finding were recorded on a set proforma according to the criteria set by WHO.

The upper tarsal conjunctiva has been selected as a convenient index of trachomatous inflammation in the eye as a whole. A classification of inflammatory disease in individual cases is developed that is based on the scoring of lymphoid follicles (F) the papillary hypertrophy (P). This intensity scale consists of four catagories severe, moderate, mild and trivial (insignificant) or absent as follows

INTENSITY	FOLLICLES	PAPILLAE
Severe	F_3	P_3
Moderate	F_3	P_2
Mild	F_2	P_0, P_1 or P_2
Trivial	F_0 or F_1	P_0, P_1 or P_2

For scaring follicles, the tarsal conjunctival surface is divided into three approximately equal zones. These zones are difined by two imaginary lines which, as renued on the ivested tarsal surface are approximately parallel amithe the upper tarsal border and curve upward towards their lateral extrimities. Zone 1 includes entire upper tarsal border and adjucent tarsal surface, zone 2 occupies this area between zones 1 and 3 and extends to the lateral quarters of lid margin, zone 3 includes the tarsal conjunctiva adjucent to control halp of the lid margin and at its centre, covers just less than half of vertical extent of tarsal surface.

F_0 - No follicles

F_1 - Follicles present, but no more than 5 in zones 2 and 3 togather.

F_2 - More than 5 follicles in zones 2 and 3 togather, but less than 5 in zones 3.

F_3 - Five or more follicles in each of 3 zones.

The scores for upper tarsal papillary hypertrophy and diffuse infiltration (P) are :-

P_0 - Absent : Normal appearance

P_1 - Minimal: individual vascular tufts (papillae) prominent, but deep subconjunctival vessels on the tarsus not obscured.

P_2 - Moderate: More prominent papillae, and normal vessels appear hazy, even when seen by the naked eye.

P_3 - Pronounced : conjunctiva thickened and opaque, normal vessels on the tarsus are hidden over more than half of the surface.

<u>Proforma for recording of findings of clinical examination</u>

Name of the school :

Name of the patient:

Age/Sex :

Standard :

Lids - Trichiasis/Entropian/ both

Lymphoid follicular hypertrophy $F_0/F_1/F_2/F_3$ as upper tarsal plate.

Papillary hypertrophy as upper tarsal $P_0/P_1/P_2/P_3$ plate.

Conjunctival scarring:

Superficial corneal vascularization

Corneal infiltration

Corneal scarring

Trachoma stage by Maccallans

Classification

Mucopurulent conjunctivitis

The scoring of symptoms and signs is done as given in the following table.

	Maximum Score	
Symptoms		
Lacrimation	3	
Discharge	3	
Grittiness	3	
Photophobia	3	
Signs		
BULBAR CONJUNCTIVA		
Hyperaemia	3	
LIMBUS		
Oedema	3	
Pannus	5	
CORNEA		
Epithelial keratitis	3	
Superficial punctate keratitis	3	
PALPABRAL CONJUNCTIVA (Score for each of 3 areas of conjunctiva, i.e. upper tarsus, upper fornix and lower lid, were recorded separately).		
Hyperaemia	3	
Diffuse infiltration	3	
Papillae	3	
Follicles -area	3	Product 9
Follicles -size	3	
Scar	3	

The analysis of clinical activity was based primarily on this degree of lymphoid follicular involvement and papillary hypertrophy on upper tarsal plate. The difinition and scaring of papillary hypertrophy proposed by fourth WHO scientific groups an trachoma was used, but the evaluation of tarsal follicles was modified as given in guide to trachoma control programme.

Stratification of cases by clinical intensity

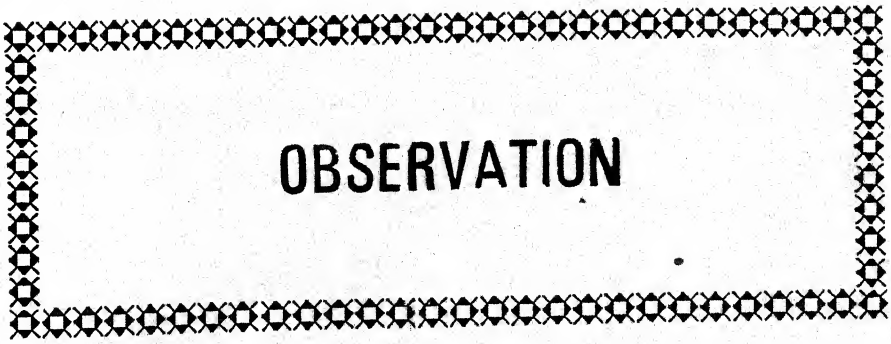
Although the patients were initially selected only on the basis of having clinically active trachoma, in analysing results, cases of trachoma were strtified in terms of clinical intensity of inflammatory disease of the conjunctiva. The stratification is based on the degree of follicle formation (F) and papillary hypertrophy (P). The ranking of four degrees of inflammatory intensity and relationship to conventional Mac Callan classification are described as follows:-

Severe trachoma Mac Callan stage IIB, III	P_3 $F_{1,2,3}$
Moderately severe trachoma Mac Callan stage I, IIA, III	P_2 , P_3
Mild trachoma Mac Callan stage I, III	P_1 , F_3 or $P_{1,2}$, F_2
In active or IInd Trachoma Mac Callan stage 0, IV	$P_{1,2}$, $F_{0,1}$

First examination was carried out for the selection of cases. The tubes of ointments marked with a code number were given to each group to be put 3 times a day of the training them well how to put the ointment. Following examination were carried out after 2, 4, 8 and 12 weeks after start of therapy.

Smears - The smears of specimens of conjunctiva were taken from everted upper tarsal part of the conjunctiva of each child following anaesthesia with one drop of 4% Xylocaine. Smears were allow to air dry and were find within 48 hours with absolute alcohol for at least 30 minutes. These specimens are brought to department of microbiology, M.L.B. Medical College, Jhansi where Geimsa staining is done and the specimens are examined for inclusion bodies.

Medication and its administration - The ointments were provided by Indian Remedies Pharmaceutical company in form of tube only marked with code numbers each containing 3 gm of 1% ointment of tetracycline or refampicin. These ointments are given to the corresponding groups with instruction that about a one centimeter long substance should be squezed out of the tube to be put in the lower forms of each eye three times per day for 6 weeks continously.


OBSERVATION

OBSERVATIONS

TABLE NO. 1

SHOWING EXAMINATION FINDINGS BEFORE TREATMENT WITH TETRACYCLINE.

Pt. No.	Age/ Sex	Follicles	Papillae	Grade	Score	Inclusion bodies
1.	2.	3.	4.	5.	6.	7.
1.	9/F	F_3	P_3	III	41	95
2.	10/M	F_3	P_2	II	36	0
3.	11/F	F_2	P_3	III	39	80
4.	10/M	F_2	P_2	II	34	0
5.	10/F	F_2	P_2	II	33	22
6.	9/M	F_3	P_2	II	30	0
7.	12/F	F_1	P_3	III	41	0
8.	11/M	F_3	P_2	II	38	0
9.	9/F	F_1	P_2	II	37	0
10.	10/M	F_3	P_3	III	39	0
11.	9/F	F_3	P_2	II	33	0
12.	12/M	F_2	P_2	II	34	0
13.	10/F	F_3	P_2	II	36	0
14.	10/M	F_2	P_3	III	44	76
15.	12/F	F_1	P_1	I	31	1
16.	9/M	F_2	P_1	I	28	0
17.	11/F	F_3	P_3	III	39	0
18.	10/M	F_2	P_2	II	34	18
19.	12/F	F_2	P_1	I	30	0
20.	10/M	F_1	P_3	III	42	56
21.	9/F	F_2	P_0	I	24	0

1.	2.	3.	4.	5.	6.	7.
22.	12/M	F_1	P_1	I	31	0
23.	10/F	F_2	P_2	II	36	0
24.	9/F	F_1	P_0	I	29	0
25.	12/F	F_3	P_2	II	32	0
26.	10/M	F_2	P_2	II	36	0
27.	9/F	F_1	P_0	I	30	0
28.	11/M	F_3	P_3	III	42	64
29.	11/F	F_2	P_1	I	31	0
30.	10/F	F_1	P_0	I	33	0
31.	10/M	F_3	P_2	II	38	0
32.	10/F	F_2	P_1	I	31	0
33.	12/M	F_2	P_2	II	40	0
34.	9/F	F_1	P_2	II	37	12
35.	9/M	F_3	P_1	I	29	0
36.	10/F	F_1	P_3	III	38	90
37.	9/M	F_1	P_1	I	27	0
38.	12/F	F_2	P_0	I	26	0
39.	10/M	F_2	P_2	II	39	0
40.	11/M	F_2	P_0	I	31	0
41.	12/M	F_2	P_3	III	31	0
42.	9/M	F_2	P_1	I	38	0
43.	10/M	F_1	P_1	I	26	0
44.	11/M	F_2	P_0	I	28	0
45.	12/M	F_3	P_3	III	30	0

1.	2.	3.	4.	5.	6.	7.
46.	10/M	F_1	P_1	I	42	0
47.	9/M	F_3	P_2	II	32	14
48.	9/M	F_2	P_0	I	36	0
49.	10/M	F_2	P_2	II	32	0
50.	12/M	F_1	P_3	III	44	93

TABLE NO. 2

SHOWING EXAMINATION FINDINGS BEFORE TREATMENT WITH RIFAMPICIN.

Pt. No.	Age/ Sex	Follicles	Papillae	Grade	Score	Inclusion bodies
1.	10/M	F_2	P_2	II	28	0
2.	9/F	F_3	P_3	III	43	94
3.	10/M	F_2	P_1	I	26	0
4.	11/M	F_1	P_2	II	32	20
5.	9/F	F_3	P_2	II	26	0
6.	12/M	F_2	P_3	III	40	78
7.	11/M	F_3	P_3	III	38	0
8.	9/F	F_3	P_2	II	34	0
9.	10/M	F_2	P_2	II	33	0
10.	12/F	F_3	P_1	I	28	0
11.	9/F	F_3	P_3	III	41	65
12.	10/M	F_2	P_2	II	36	0
13.	12/F	F_1	P_3	III	36	0
14.	9/M	F_2	P_0	I	22	0
15.	10/F	F_3	P_2	II	32	18
16.	10/M	F_3	P_3	III	39	91
17.	12/F	F_2	P_1	I	29	0
18.	10/M	F_3	P_2	II	26	0
19.	9/F	F_2	P_3	III	43	56
20.	10/M	F_3	P_3	III	41	0
21.	9/M	F_2	P_2	II	36	0

1.	2.	3.	4.	5.	6.	7.
22.	12/F	F_1	P_2	II	38	0
23.	9/M	F_1	P_3	III	37	0
24.	12/M	F_3	P_1	I	24	0
25.	10/F	F_2	P_2	II	39	15
26.	9/F	F_3	P_1	I	28	0
27.	10/M	F_2	P_2	II	30	0
28.	12/F	F_3	P_3	III	39	85
29.	13/M	F_1	P_0	I	24	0
30.	13/M	F_1	P_1	I	30	0
31.	10/M	F_2	P_1	I	28	0
32.	9/F	F_3	P_3	III	42	92
33.	9/F	F_2	P_2	II	27	0
34.	10/M	F_3	P_2	II	34	0
35.	9/F	F_3	P_2	II	36	0
36.	10/F	F_2	P_3	III	41	0
37.	12/M	F_3	P_2	II	38	0
38.	11/M	F_3	P_2	II	37	0
39.	12/F	F_2	P_2	II	34	0
40.	9/M	F_3	P_2	II	30	0
41.	12/F	F_1	P_2	II	28	12
42.	13/M	F_2	P_2	II	29	0
43.	9/M	F_3	P_3	III	44	62
44.	10/M	F_2	P_2	II	38	0
45.	9/M	F_3	P_2	II	39	0

DIAGRAM 1 : SHOWING INCIDENCE OF TRACHOMA

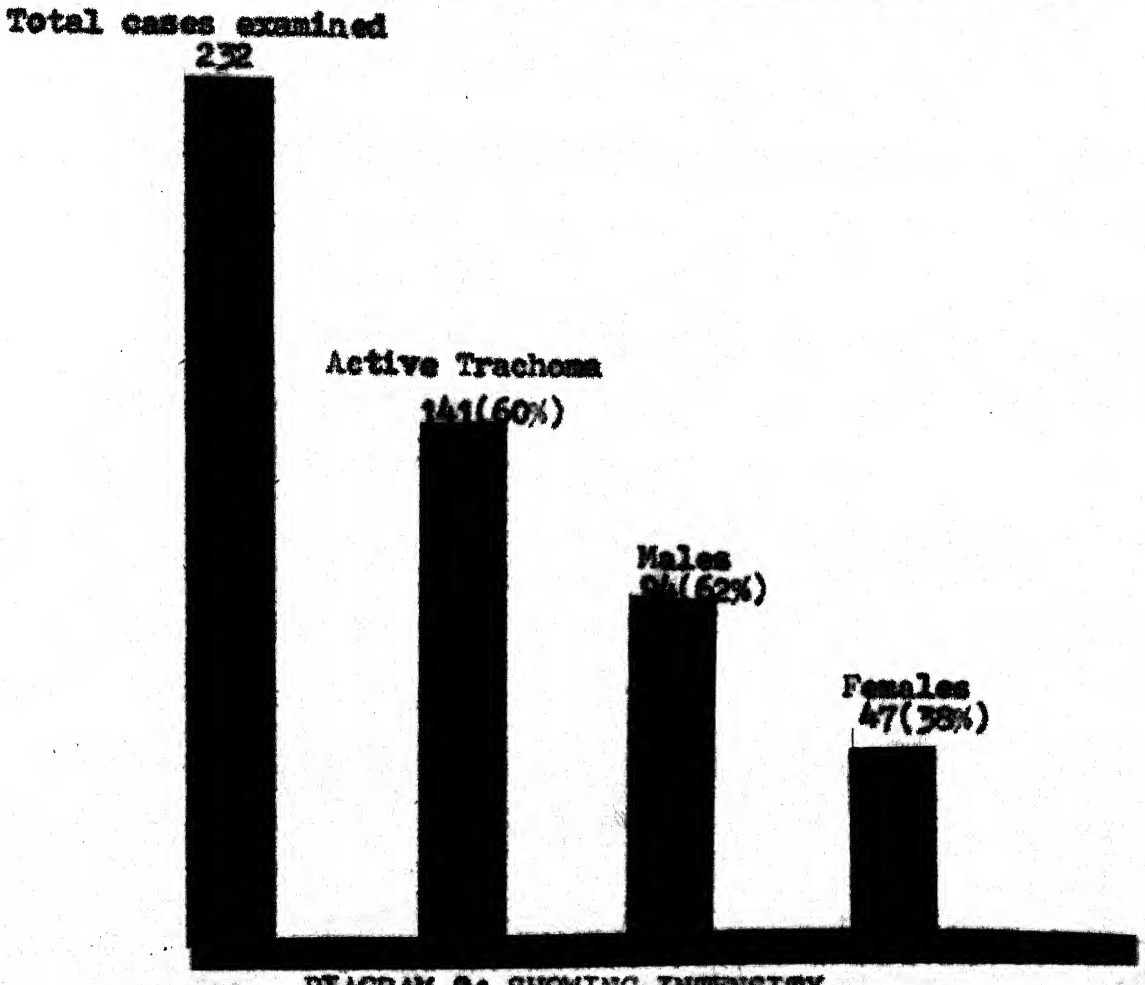
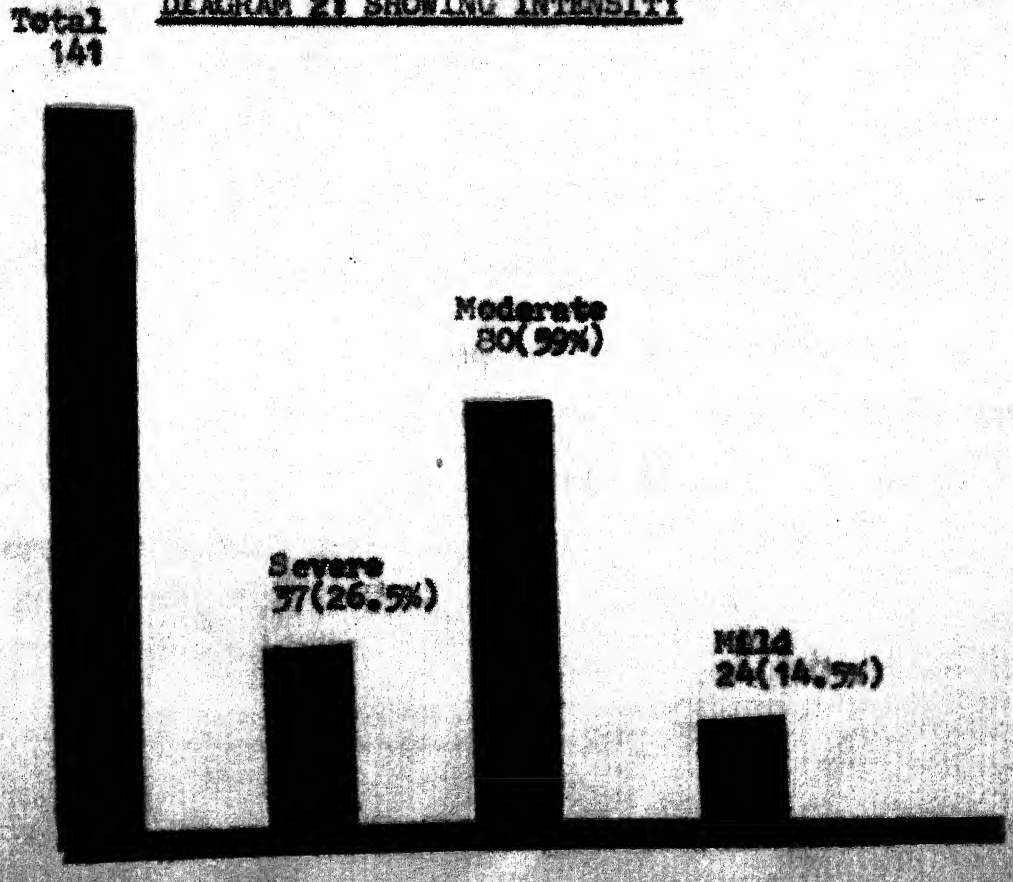


DIAGRAM 2: SHOWING INTENSITY



Of the 232 patients examined 141 (60%) were found havigg active trachoma in various stages. Out of these 37 (26.5%) were having severe trachoma, 80 (59%) had trachoma of moderate intensity and rest 24 (14.5%) had trachoma of mild intensity. These findings are shown in diagram No.1. Patients were ranging 8-13 years in age. 94 (62%) were male and 47 (38%) were female.

The 100 cases selected for study consisting of 59 (59%) males and 41 (41%) females. Out of these 25 (25%) were having trachoma of severe intensity, 58 (58%) were having trachoma of moderate intensity and 17 (17%) had trachoma of mild intensity on shown in diagram No. 2.

The patient group selected to be treated with tetracycline eye ointment were having 12 (24%) cases of severe trachoma, 30 (60%) cases of moderate intensity of trachoma and 8 (16%) of mild intensity of trachoma. This population group no consisted of 29 male and 21 female patients.

Another 50 cases selected for treatment with Rifampicin eye ointment, consisted of 13 (26%) cases having severe trachoma, 28 (56%) moderate trachoma and 9 (18%) were having mild trachoma.

DIAGRAM 3: SHOWING SEX INCIDENCE

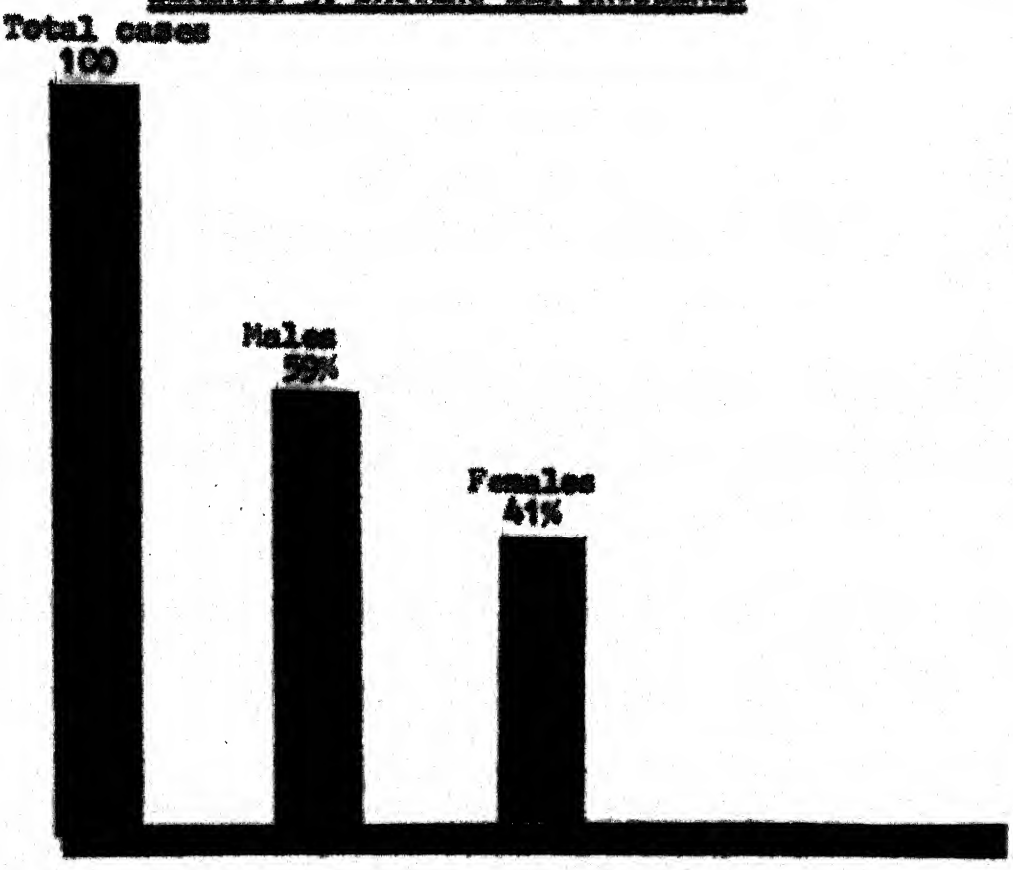


DIAGRAM 4 : SHOWING INTENSITY

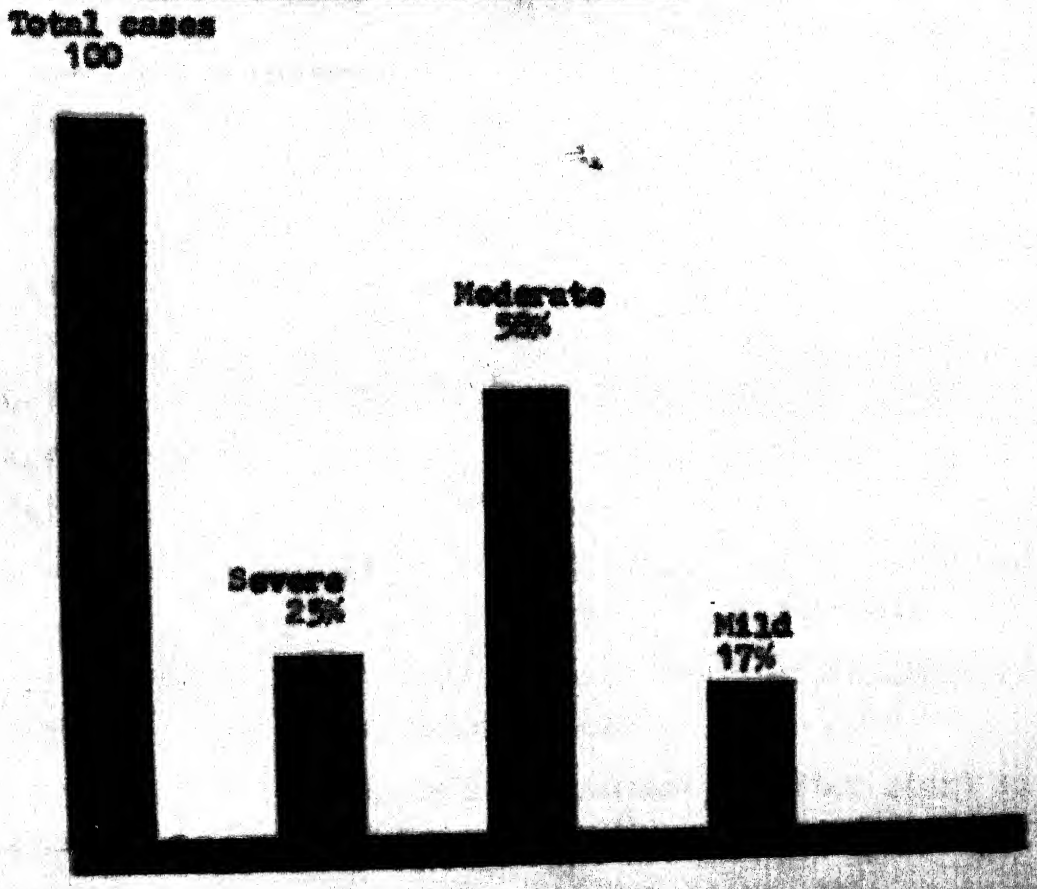


TABLE NO. 3

SHOWING INTENSITY AND SEX INCIDENCE

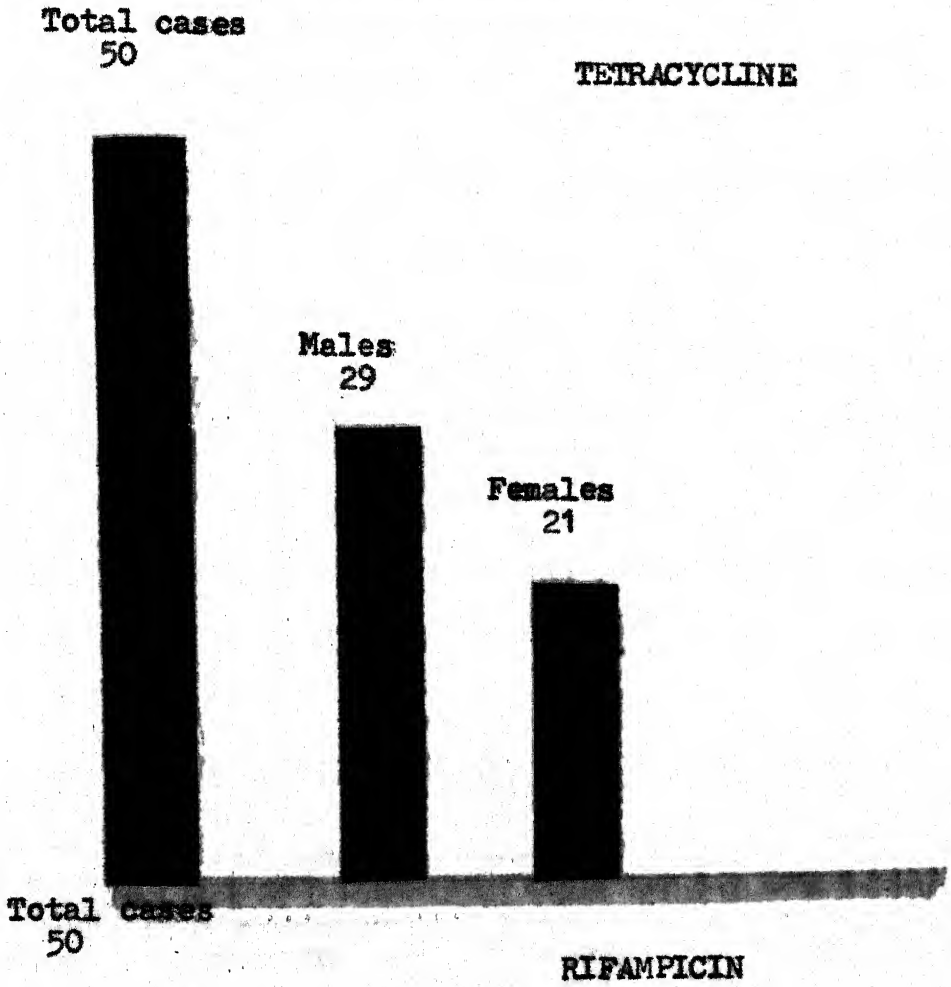
Treatment Group	Total No.of patients	Intensity Grade			Sex incidence	
		Severe	Moderate	Mild	Male	Female
Tetracycline	50	12 (24%)	30 (60%)	8 (16%)	29 (58%)	21 (42%)
Rifampicin	50	13 (26%)	28 (56%)	9 (18%)	30 (60%)	20 (40%)

TABLE NO. 4

TABLE SHOWING THE TREATMENT SCHEDULE

DATES	EXAMINATION	TIME OF EXAM. IN WEEKS
14.10.83 to 20.10.83	Initial examination	6,before treatment
26.11.83 to 28.11.83	Geimsa Smears	1,before treatment
2.12.83 to 16.1.84	Treatment and clinical examination	0-6,after start of treatment
16.12.83 to 12.1. 84	Clinical examination and Geimsa smears	2,after start of treatment.
3.1.84 to 5.1.84	Clinical examination and Geimsa smears	4,after start of treatment.
17.1.84 to 20.1.84	Clinical examination and Geimsa Smears	6,after start of treatment.
3.2.84 to 5.2.84	Clinical examination and Geimsa smears	8,after start of treatment.
5.3.84 to 8.3.84	Clinical examination and Geimsa smears	12,after start of treatment.

DIAGRAM 5 : SHOWING SEX INCIDENCE



The above table is showing the work schedule. Initial clinical examination is carried out 6 weeks before treatment in the month of October, 1983. In another visit the smears are prepared from the selected group of 100 patients for Geimsa staining in the month of November, 1983 The treatment is started simultaneously in both groups from 2nd December, 1983 upto 16th January, 1984 for 6 weeks. Clinical examinations are carried out after 2, 4, 6, 8 and 12 weeks of treatment. The smears for Geimsa staining were also prepared.

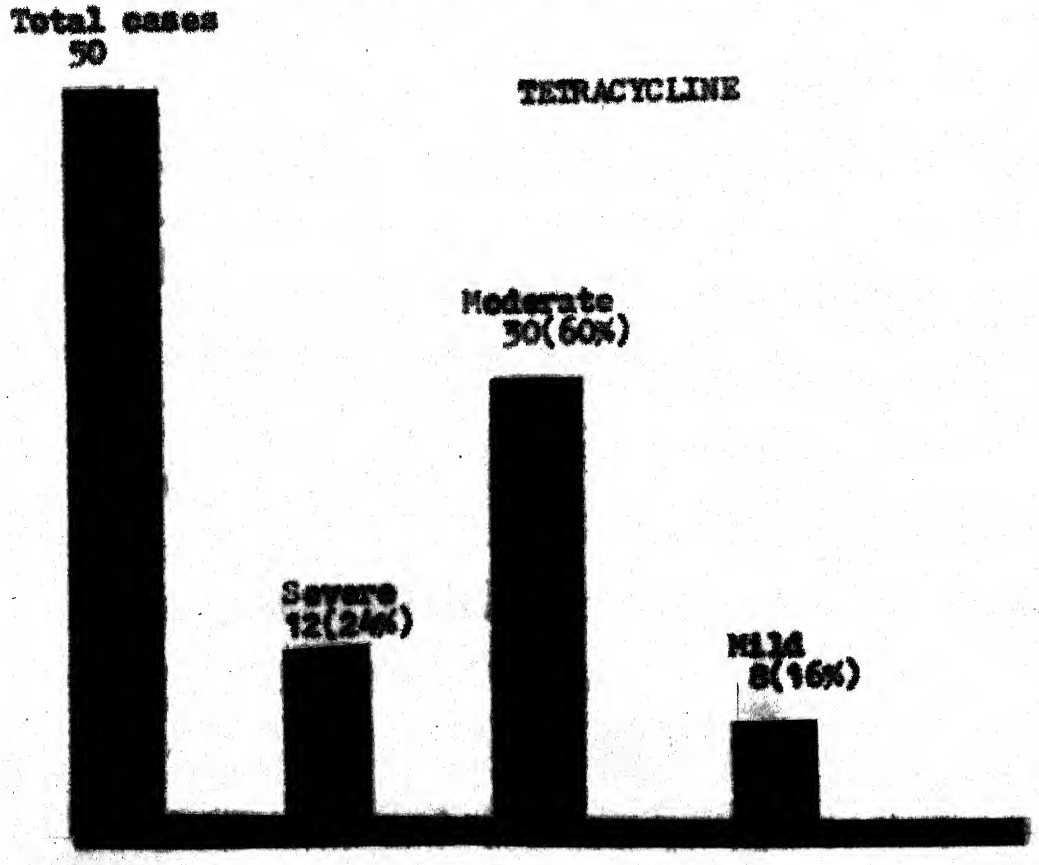
TABLE NO. 5

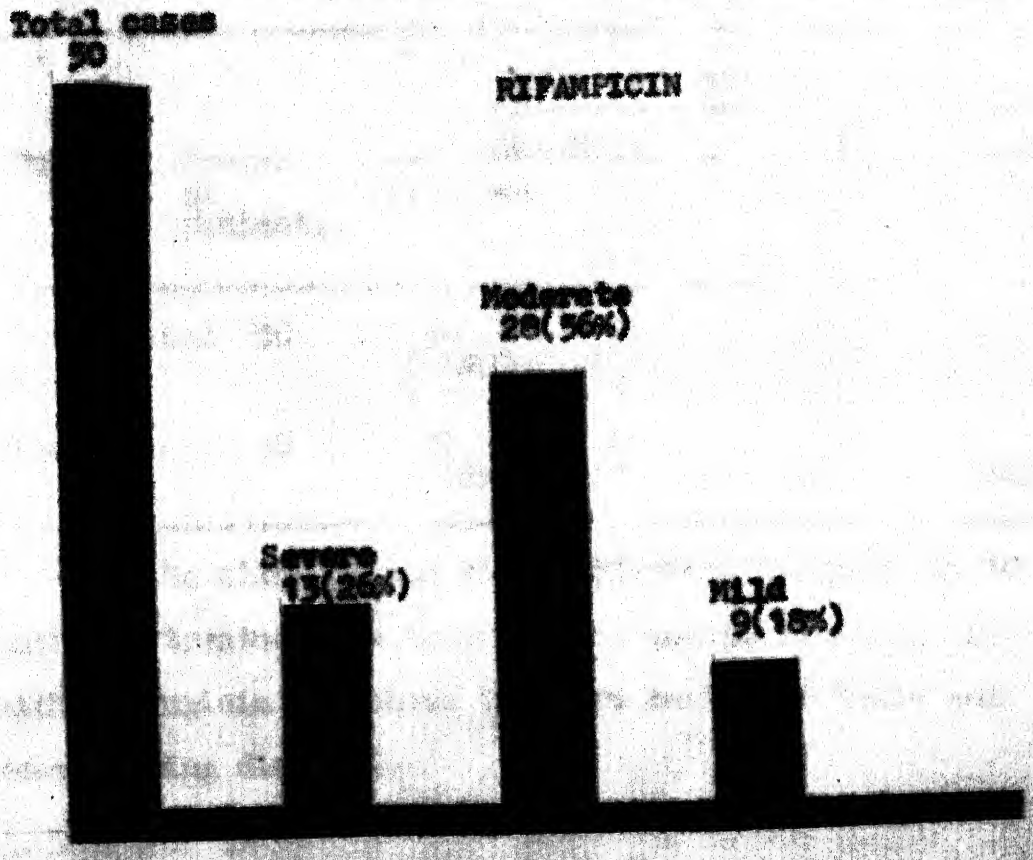
SHOWING GEIMSA STAINED SMEARS

Disease intensity	Number of smears examined	Number positive	Percentage positive	Range of number of inclusions	Geometric mean
Severe	25	15	60	0-94	7
Moderate	58	7	12	0-22	5
Mild or non active	17	-	-	0	0

The above mentioned table is showing the presence of inclusion bodies in Geimsa stained smears in the patients, before start of treatment. In the 25 cases having severe degree of trachoma 15 smears were positive for inclusion bodies constituting the 60%. The number of inclusion bodies ranged from 0-94 per positive smear and average was 7 inclusion bodies per smear examined.

DIAGRAM 6 : SHOWING INTENSITY





Out of 58 smear of the patients having moderate severity of trachoma 7 smears were positive for inclusion bodies making the 12% incidence. The number of inclusion bodies ranged from 0-22 constituting an average of 5 inclusion bodies per smear examined.

In 17 smears of mild or non active group of patients no smear was positive for inclusion bodies.

The smears with many inclusions were more common in patients with severe disease.

TABLE NO. 6

SHOWING EFFECT OF TREATMENT

Drugs	Number of patients	Number of patients cured			
		6 weeks		12 weeks	
		Clinical	Microbiological	Clinical	Microbiological
Tetracycline	50	44 (88%)	47 (94%)	40 (80%)	46 (92%)
Rifampicin	50	38 (76%)	46 (92%)	37 (74%)	38 (76%)

The clinical and microbiological findings in 50 patients treated with tetracycline and 50 patients treated with Rifampicin are shown in above mentioned table and accompanying diagram.

The average clinical scores in the group treated with tetracycline were 34 and in the group treated with Rifampicin were 36. After one week of treatment there was marked decrease in the clinical scores in both groups. The average clinical scores in these patients immediately after completion of treatment for 6 weeks was 8 for tetracycline group and 9 for rifampicin group.

Clinical examination at 12 weeks showed complete cure in 40(80%) out of 50 patients treated with tetracycline and 37(74%) out of 50 patients treated with rifampicin.

The distribution of inclusion positive cases and average distribution was almost similar in both groups. After 4 weeks of treatment no positive smear was found in tetracycline group while only 2 positive smears were found in Rifampicin group.

The beneficial effect of therapy with two antibiotics were statistically significant ($p < 0.001$) but there was no difference in the efficacy of two drugs ($p > 0.2$) there was marked improvement in the clinical condition of the patients who were not cured with tetracycline or rifampicin therapy.

DISCUSSION

DISCUSSION

This study was designed to test the relative efficiency of tetracycline and rifampicin as 1% eye ointments administered under conditions and dosage schedule possible in many developing countries, that is treatment is limited to school children and given thrice daily. In this double blind treatment trial stratified randomization for grades and intensity of inflammatory responses, age and sex produced a well balanced distribution of patients in groups allocated to treatment with tetracycline and rifampicin.

In the recent study the whole conjunctiva including upper tarsal area was examined assessing the presence and intensity of inflammatory changes. Daraugar S. et al. in 1980 found in their studies of trachoma and paratrachoma that (1) in the whole conjunctiva the intensity of inflammatory responses is heigher than in upper tarsal conjunctiva. (2) after treatment the cure rate for whole conjunctiva is markedly lower than rate for upper tarsal conjunctiva and (3) in some patients with cured upper tarsal conjunctiva an active but mild to moderate disease could be found in upper and lower conjunctiva for nices. It was found that this residual disease can cause recurrence in treated cases.

In this study the follow up investigations were carried out for upto 6 weeks after completion of treatment. In a present study by Daraugar et al in 1977 it is found that clinical and microbiological recurrence generally occur within 6 weeks after completion of treatment.

The results of this investigation show that topical therapy of trachoma with tetracycline or rifampicin eye ointment three times daily for 6 weeks is heightly effective. Rifampicin produced clinical and microbiological cure rates of 75% and 96% respectively. These results are almost equal to those obtained by Daraugar, S et al in 1977. Tetracycline has also produced a very height clinical and microbiological cure rates of 80% and 93% respectively.

In this trial between 20-25% of patients were not cured clinically after treatment with either tetracycline or rifampicin. Although an initial clinical improvement was observed in all the cases moderate to severe recurrences were observed in only 3 patients (6%) treated with tetracycline and 5 patients (10%) treated with rifampicin. While it is possible that drug resistance may have developed in these cases no attempt is made to investigate thi s. In a previous study by Daraugar S. and Viswalingam, N et al. It is found that resistance to rifampicin had not developed in Chlamidia trachomatis isolates obtained from the

the patients who were not cured with this drugs. It is possible therefore that inadequate application of eye ointment may be responsible for these failures.

While two antibiotics significantly improved the disease condition rifampicin did not appear to offer any significant advantage over tetracycline. In a study Becker, Y. found in 1972 that laboratory evidence indicate that the trachoma agent (chalumidia trachomatis is specifically inhibited by rifampicin even when briefly exposed during the non riplicating phase of organism. However keshishyan, H. et al found in 1973 that chlaumidia strains rapidly develops resistance to rifampicin in laboratory system, while there was no evidence of such resistance in this study, the possible emergence of resistance chlamidia strains would certainly limit the usefulness of drug in repitetive mass treatment programs.

In evaluating the results of trachoma chemotherapy, was found that prevalence of trachoma agent appeared is change readily than clinical disease. While clinical intensitity of inflammatory disease has not been directly related to the subsequent occurance of blinding complications, trichiasis, entropian, corneal scarring and dry eye syndromes. Epidemiological studies suggest a strong correlation.

Since the aim of chemotherapy is prevention of visual loss, the effect of antibiotics on the clinical intensity of disease is the most direct way to evaluate the efficacy of treatment.

As in other areas of world, Africa, middle east where trachoma as indemic seasonal epidemics of purulant conjunctivitis to occur in this village in the late summaer and autumn. While it is widely accepted that thus concurrent bacterial infection contributes to the severity of trachoma, the exact machanism is still uncertains.

Treatment had the effect of altering the effect of altering the disease temporarily but did not affect the individuals course in long run, presumably because the factors in the childs environment that produce disease has not changed since the school children are heavily infected in this community, reinfection with trachoma agents and bacterial pathogens may be common. Only chemotherapy on a community wide basis would be expected to have a significant effect on this process. Other methods of improving the environment such as introduction of piped water into the houses could also influence the disease process and these measures should be considered in trachoma controle programmes.

The topical applications of antibiotics no relatively inefficient although safe. Systemic sulfonamides or antibiotics have been effective in mild trachoma as seen in studies carried out by Dawson, C.R.et al in 1967 and 71 on American Indians. The use of orally administered drugs such as tetracyclines or sulfonamides in hyper endemic trachoma areas poses many problems. Among these are the occurance of toxic effects in children and the almost certain possibility of producing an antibiotic resistance among intestinal bacterial pathogens that are respobsible for death and morbidity in diveloping countries. One solution to the dilemma would be the use of occular drug dilivery divices that provide heigh antibiotic levels in the conjunctiva but not significant systemic doses.

Mass antibiotic treatment programmes for trachoma controle sgems to be associated with milder disease and a reduction in blinding complications. However the advancement of economic progress is uncertain in these areas where trachoma still causes visual disability. Moreover the damage caused by trachoma may occur in first ten years of life so that many individuals will develop complications lateron even though the disease may have become milder in the community. Thus even in short run the antibiotic treatment programmes are needed to reduce the occurance of complications.

CONCLUSIONS

CONCLUSION

The present study is undertaken to compare the effect of tetracycline and rifampicine as 1% eye ointment in topical therapy of trachoma cases.

1. Out of 232 patients examined 141 were the cases of active trachoma showing the 60% incidence of trachoma.
2. Severity of the trachoma is found to be 26.5% (37 cases) of severe degree, 59% (80 cases) of moderate degree and 14.5% (24 cases) of mild degree.
3. The microbiological intensity of disease as measured by the prevalence and amount of trachoma agent corresponded with the clinical findings.
4. In Geimsa stained smears the patients with severe trachoma had a heigh prevalence of inclusion positive smears (60%) but only 12% of the patients with moderately active disease were inclusion positive. Again the smears with many inclusions were more common in patients with severe disease .
5. The average clinical scores before treatment in the group treated with tetracycline were '34' and in group treated with rifampicin were '36'.
6. After one week of treatment there was a marked decrease in the clinical scores in both groups. The average clinical scores in these patients immediately after completion of treatment of 6 weeks was 8 for tetracycline and 9 for rifampicin.

7. Clinical examination at 12 weeks showed complete cure in 40(80%) out of 50 patients treated with tetracycline and 37(74%) out of 50 patients treated with rifampicin.

8. The beneficial effect of therapy with two antibiotics were statistically significant ($P < 0.001$) but there was no difference in the efficiency of two drugs ($p > 0.2$).

9. There was a marked improvement in the clinical condition of the patients who were not cured with tetracycline or rifampicin therapy.

10. The distribution of inclusion positive cases and average distribution was almost similar in both groups after four weeks of treatment, no positive smear found in tetracycline groups, while only two positive cases were found in rifampicin group.

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